Diabetic Nephropathy and Intervention in Unani System of Medicine

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***Abstract*-Context: Diabetic nephropathy (zoafe kulya bawajah ziabetes shakari) is kidney disease or damage that results as a complication of diabetes. The exact cause of diabetic nephropathy is unknown, but it is believed that uncontrolled high blood sugar leads to the development of kidney damage,especially when high blood pressure is also present. In some cases, genes or family history may also play a role. Not all persons with diabetes develop this condition.Each kidney is made of hundreds of thousands of filtering units called nephrons. Each nephron has a cluster of tiny blood vessels called a glomerulus. Together these structures help remove waste from the body. Too much blood sugar can damage these structures, causing them to thicken and become scarred. Slowly, over time, more and more blood vessels are destroyed. The kidney structures begin to leak and protein (albumin) begins to pass into the urine.Clinically, DN is characterized by a progressive increase in proteinuria and decline in GFR,hypertension, and a high risk of cardiovascular morbidity and mortality.The earliest clinical evidence of nephropathy is the appearance of low but abnormal levels(>30 mg/day) of albumin in the urine, referred to as microalbuminuria, and patients with microalbuminuria are referred to as having incipient nephropathy. Diabetic nephropathy is a leading cause of end stage renal failure. The pathogenesis of diabetic nephropathy is multifactorial with contribution from metabolic abnormalities, homodynamic alteration, and various growth factors and genetic factors. Epidemiologic and family studies have demonstrated that family clustering and ethnicity plays an important role in the risk of developing this kidney disease1. It is estimated that up to 50% patients with diabetes mellitus will develop renal failure2. It is now firmly established that diabetic nephropathy is associated with high morbidity and mortality3. There is marked heterogeneity in the clinical picture seen in long termed diabetes as some diabetic patients even with poor metabolic control may not develop clinical diabetic nephropathy4.Ancient Unani physicians estimated kidneys as pivotal organ and zoafe kulya is a secondary disease to absorb and filter the urine from blood i.e. blood purification. The current study is taken for the first time and considers the assessment of the scientific validity of the Unani medicines by applying modern parameters.**

I. Risk Factors for Development and Progression of Diabetic Nephropathy

Before the widespread aggressive treatment of blood pressure and hyperglycaemia, between 25% and 40% of both type 1 and type 2 patients developed diabetic nephropathy over the course of 25 years5,6,7 and risk factors that differentiate this subgroup from patients who maintain normal renal function are systemic hypertension, glycaemic control, gender (M>F), genetic factors,hyperlipidaemia, dietary protein intake and smoking.

II. Blood Pressure

Hypertension is much more common amongst diabetic patients than
in the general population and has been identified as a major risk factor for both macrovascular and microvascular complications including diabetic nephropathy. Total cardiovascular mortality in diabetes is strongly associated with raised blood pressure, particularly in type 2 disease.Hypertension is strongly associated with insulin resistance, even in the absence of diabetes,and some 40-70% of type 2 patients will become hypertensive during their disease8. Only 25% of patients with type 1 diabetes are hypertensive and many of these will already have microalbuminuria or overt nephropathy9. Nevertheless, in both type 1 and type 2 diabetes with overt nephropathy the rate of decline of renal function correlates strongly with hypertension10,11 and in microalbuminuric patients hypertension correlates with the degree of albuminuria12. In both these situations antihypertensive therapy is beneficial. Furthermore in normoalbuminuric type 1 diabetes small increases in blood pressure have been correlated with the subsequent development of microalbuminuria13. Therecan therefore now be little doubt that a raised blood pressure is a risk factor for the development and progression of diabetic nephropathy as well as a potent risk factor for cardiovascular morbidity and mortality.

Glycaemic control

Type 1 and type 2 diabetes have in common the state of chronic hyperglycaemia, and glucose-dependent processes are likely to be involved in the pathogenesis of diabetic complications,including nephropathy. Glucose- induced tissue injury may be mediated by the generation of advanced glycated proteins or via other mechanisms such as the polyol pathway, both of which have been implicated in nephropathy14. Consistent with this hypothesis are observational studies correlating haemoglobin A1c (HbA1c) concentration with the development and progression of microalbuminuria and overt nephropathy13.

Proteinuria

Proteinuria is generally regarded as a marker for the degree of glomerular damage: the level of proteinuria correlates well with the prognosis for renal function, and interventions that retard the progression of diabetic renal disease also reduce proteinuria. However, we do not yet know whether the flux of protein across the glomerular basement membrane is causally implicated in the evolution

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of diabetic renal disease or simply reflects glomerular damage15.

Genetic factors

Genetic factors are likely to be important in diabetic nephropathy. Recent interest has focused on genes of the renin angiotensin system, which are known to be highly polymorphic and have been extensively studied in relation to cardiovascular disease. An insertion(1)/ deletion(D) polymorphism in the ACE gene has been identified that is strongly associated with raised circulating ACE levels and with increased risk of coronary heart disease in non-diabetic individuals. Some studies have found the DD genotype to be associated with an increased risk of diabetic nephropathy and a rapid decline of GFR in both type 1 and type 2 diabetes16. The clinical implications have yet to be explored. Other genetic loci that may be involved include the sodium lithium exchanger and the sodium—hydrogen antiporter genes.

Hyperlipidaemia

Hyperlipidaemia is common in both type 1 and type 2 diabetes. Raised plasma triglycerides and low levels of highdensity liproproteins (HDL) have been correlated with the development of diabeticnephropathy as well as with cardiovascular diabetic complications5,17,18. Triglyceride and cholesterolreduction, although important in reducing cardiovascular risk, has not been found to alter the progression of renal disease and the importance of hyperlipidaemia remains to be established in this respect.

III. Material & Methods

35 patients of type 2DM with clinical Nephropathy were taken at TDF (TRIAL DRUG FORMULA) for 120 days & creatinine clearance test was repeated for every 30 days. TDF,especially prepared with the aim to modulate impaired kidney function contains musaffi,muhallil, mufattah and mudir advia.Different hospitals were visited from January 2009 to May 2009 for the collection of data.Patients were also visited at their homes for this purpose. Data was collected from priti hosp.Allahabad, SUMC Hospital Allahabad, and from Himmatganj Allahabad U.P.A total of 54 patients were interviewed for data collection, of which, 31 were males and 23 were females. Specific questionnaire was used which included variety of questions, such aspresent age of the patient, age at diagnosis of nephropathy, age at diagnosis of diabetes,total duration of diabetes, familial relationship between husband and wife, familial relationship between the parents of patients, family history regarding the same or any other disease,information regarding different clinical tests done for the diagnosis of nephropathy andinformation about the socio economic status (occupation), education and life style of thepatients.

Height and weight of the patients were studied in order to check their link with theprevalence of disease. Height was measured in meters while weight was recorded in kg.Clinical tests included blood urea, serum creatinine, blood glucose, sodium, potassium, and albumin. Statistical analysis like mean, standard error, number of studied samples (n), t-test and percentage (%) were also carried out during our study. For control studies regarding diabetes and diabetic nephropathy, 20 normal subjects were interviewed to have a complete comparative analysis.

Result: After 120 days

1. In 65.71 % patients with mild and moderate renal impairment normal creatinine clearance was obtained.
2. In patients with severe renal impairment slow apparent response was seen.

IV. Discussion

During present investigations, of the total diabetes patients examined, 35 (64.81%)were diagnosed as type 2 diabetes. Among type 2 diabetes patients 19 (54.29%) were males and 16 (45.71%) were females. Mean present age of male type 2 patients was 62.36±0.59 years, and that of females was 65.28±0.68 years, while for both the sexes it was 63.66±0.45 years. The age at diagnosis of diabetic nephropathy in male patients was 60.24±0.70 years, and in female patients was 62.71±0.60 years and it was 61.64±0.48 years for both the sexes. Diabetes in all type 2 patients was diagnosed at 47.12±0.33 years. In male type 2 patients diabetes was diagnosed at 46.09±0.43 years and in female patients at 48.41±0.49 years. The duration of diabetes in type 2 patients was 14.20±0.20 years after which they were diagnosed diabetic nephropathy. The duration of diabetes in male patients was 14.12±0.27 years and in female patients was 14.29±0.29 years. The total duration of diabetes in type 2 patients was 16.48±0.24 years, and in male patients the total duration was 16.17±0.33 years while in female patients it was 16.88±0.36 years. Mean body mass index (BMI) in type 2 patients was 26.77±0.15 kg/m2. Mean BMI in male patients was 25.57±0.16 kg/m2, and in female patients it was 28.27±0.21 kg/m2. In the control sample, BMI in males was 24.69±0.17 kg/m2 and in females 26.05±0.19 kg/m2. The difference of mean BMI in male and female patients compared to control males and females was 2.22 and 0.88 kg/m2.Biochemical analysis of type 2 patients included blood urea, creatinine, blood glucose,sodium and potassium level. Their mean values are shown in [Table 1].The highest percentage 51.43% was of those patients who have not obtained any school education, and the lowest percentage 5.71% of those who had education of university level. The socioeconomic status of patients also effect development of diabetes and DN. According to investigations, low income employees and small shopkeepers are mostly affected with diabetes. Results from the present study also agree with the above results. Most of the low-income patients (shopkeepers, farmers and laborers) develop DN.[19] Socioeconomic status (occupations) wise distribution of type 2 patients is given in[Table 3].The highest percentage of patients was in the skilled (nonmanual) category (22.86%);next highest category was of partly skilled (20%), while the lowest percentage of patients was in unskilled (11.43%) category.

V. TRIAL DRUG FORMULA

Dar Hald (Berberis vulgaris), Mako20,21 (Solanum nigrum), Vaj (Acorus calamus), Majeth (Rubia cordifolia), Panchang (Chena podium album), Zaravand (Arista lochia), Gokhru20,21,22,23(Tribulus terr), Pakhan Baid (Saxitraga lingulata), Chandan (Satalum Album) in equal amount and given in powder form at a dose of 3 gm two times daily with decoction of Tukhm Khayareen, Tukhm Gazr, Tukhm Karfas, Chiraita, Sarphoka, Jadwar, Jaifal, Behman surkh, Fil fil siyah, Mako21,23,24, Kasini each 3gm.

VI. CONCLUSION

This formulation acts as a normohomeostatic agent by modulating the renal clearance function through vasodilatation and improve blood flow. During initial stages there is quick modulation of renal clearance function. So it is recommended to start this formulation in early stages. Therefore it can be stated that the above formulation is an effective, affordable treatment for Diabetic Nephropathy and is free from adverse effects.

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Table 1: Biochemical Analysis of type 2 Diabetes Patients

	Sex	Mean	S.E	n
Blood Urea (mg/dl)	M	155.65	1.84	20
	F	156.58	2.46	15
	Both	156.02	1.48	35
Serum Creatinine (mg/dl)	M	6.83	.09	19
	F	7.04	.07	16
	Both	6.91	.06	35
Blood Glucose (mg/dl)	M	336.33	4.58	26
	F	343.22	4.87	23
	Both	339.39	3.34	49
Sodium (Mmol/Lit)	M	157.93	0.93	22
	F	156.55	1.41	15
	Both	157.44	0.77	37
Potassium (Mmol/Lit)	M	6.84	0.08	22
	F	6.76	0.11	13
	Both	6.81	0.06	35

Distribution of type 2 patients according to levels of education they had attained is shown .

Table 2 Distribution of type 2 Nephropathy in Relation to Level of Education

Education	Number	Percentage
None	18	51.43
School	10	28.57
College	5	14.29
University	2	5.71

Table 3 Distribution of Type 2 Diabetes in Relation to Socioeconomic Status

Occupation	Number	Percentage
Professional and managerial	6	17.14
Intermediate		
Skilled (Non manual)	5	14.29
Skilled (Manual)	8	22.86
Partly Skilled	5	14.29
Unskilled	7	20.00
	4	11.43